JUN 13 2005

510(k) SUMMARY OF SAFETY AND EFFECTIVENESS
BNP Assay for Bayer ADVIA® Integrated Modular System (IMS)

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of the Safe Medical Device Act of 1990 and 21 CFR 807.92.

The assigned 510(k) number is: k051265

June 6, 2005

1. Submitter's name, address and telephone number:

Andres Holle
Manager, Regulatory Affairs
Bayer HealthCare LLC
A subsidiary of Bayer Corporation
511 Benedict Avenue
Tarrytown, NY 10591
TEL: 914-524-2531
FAX: 914-524-2500
Email: andres.holle.b@bayer.com

2. Name of the device:

a) Classification Names: B-type natriuretic peptide test systems, §862.1117
Classification: Class II
Product Code: NBC

b) Common name: BNP assays

c) Proprietary name: ADVIA Immuno Modular System (IMS)®
B-Type Natriuretic Peptide (BNP) Assay

d) The device:

Product Name	Reagent Part # / BAN Number	Calibrator Part # / BAN Number
ADVIA IMS BNP Assay	0154537 (100 tests)	00155177

3. Predicate Device:

Product Name	Reagent Part #	Master Curve Material Part #
ADVIA Centaur BNP Assay	REF 02816634 (500 tests) REF 02816138 (100 tests)	REF 02815905

4. Description of the device:

The ADVIA IMS BNP Assay is an *in vitro* immunoassay intended for the quantitative measurement of b-type natriuretic peptide (BNP) in human EDTA plasma covering the analytical range of 10 to approximately 6,000 pg/mL. The assay is a heterogeneous sandwich immunoassay using magnetic separation. Reagent 1 (R1) contains monoclonal antibody to BNP labeled with FITC and Reagent 2 (R2) contains the second monoclonal antibody to BNP (F(ab)2) conjugated to the enzyme alkaline phosphatase (ALP). The monoclonal antibodies used in the ADVIA IMS BNP assay are identical to those used in the ADVIA Centaur assay. The sandwich complex formed by the analyte and the antibody conjugates is captured by the magnetic particles so that the BNP concentration in the sample can be measured in terms of enzyme activity. The substrate used for this assay is a dioxetane phosphate derivative, which is dephosphorylated by ALP resulting in photon emission. Luminescence is measured by a photomultiplier tube. The dose response curve is proportional to the analyte concentration in sample.

The Centaur BNP Master Curve Material (MCM) (part number 02815905) will be used as the calibrators (six levels) for the ADVIA IMS BNP assay. The controls used in the ADVIA IMS BNP assay, QC BNP 1, 2, 3 (REF 02817045), are existing Bayer Centaur products consisting of three levels of lyophilized controls. The controls contain various concentrations of BNP in buffered sodium caseinate with preservative.

5. Intended Use

For *in vitro* diagnostic use in the quantitative determination of B-type Natriuretic Peptide (BNP) in human plasma using the ADVIA IMS® System. This assay is indicated for the measurement of plasma BNP as an aid in the diagnosis and assessment of the severity of heart failure. In patients with acute coronary syndromes (ACS), this test, in conjunction with other known risk factors, can also be used to predict survival as well as to predict the likelihood of future heart failure. This assay is not intended for use on any other system.

6. Similarities and Differences between ADVIA® IMS™ BNP assay and Bayer Centaur® BNP assay:

	ADVIA IMS BNP assay	***ADVIA Centaur BNP assay*** *(predicate device)*
Intended Use	Same	Same
Summary	Same	Same
Principle	Heterogeneous Sandwich Magnetic Separation Assay	Heterogeneous Sandwich Magnetic Separation Assay
Reagents	Two liquid reagents contained in system specific packaging	Two liquid reagents contained in system specific packaging
Storage	2-8 °C	2-8 °C
Stability	Same	Same
Precautions	Same	Similar
Indications of Deterioration	Same	Same
Performance Characteristics	Same	Same
Limitations	Same	Same
Parameters	Multi-point calibration, sandwich immunoassay and system specific parameters	Multi-point calibration, sandwich immunoassay and system specific parameters

7.

7. Performance summary:

a) Imprecision:

ADVIA IMS	
Level (pg/mL)	Total CV(%)
71	4.1
716	1.9
2660	1.8

ADVIA Centaur	
Level (pg/mL)	Total CV(%)
48.5	3.5
458	2.8
1736	2.9

b). Correlation:

Specimen type	Comparison System (X)	N	Regression Equation	Syx (pg/mL)	R	Sample Range (pg/mL)
EDTA Plasma	ADVIA Centaur	360	0.990 * X + 4.37	111.7	0.992	4 to 4531

(Y= ADVIA IMS, X= comparison system)

c) Interfering substances:

Interference	Interference Conc. mg/dL	Recovery (pg/mL) Expected	Observed	% Deviation
Albumin	**7,000**	145.3	131.5	-9.46
		407.5	377.9	-7.27
Bilirubin	**25**	79.4	80.6	1.50
		366.1	356.4	-2.65
Cholesterol	**1,000**	133.8	139.5	4.26
		352.8	383.6	8.73
Creatinine	**2.5**	99.2	100.0	0.76
		427.0	419.0	-1.87
Hemoglobin	**750**	86.7	78.3	-9.68
		402.3	366.7	-8.86
Triglyceride	**800**	86.2	83.4	-3.19
		389.4	384.3	-1.32
Urea Nitrogen	**200**	87.7	88.9	1.34
		380.2	382.0	0.48
IgG	**4,600**	129.3	141.2	9.15
		398.7	435.8	9.30

d). Analytical Range:

4 pg/mL (1.1 pmol/L) to calibrator level 6 concentration (about 6000 pg/mL or 1728 pmol/L)

e) Minimum Detectable Concentration:

ADVIA IMS BNP (pg/mL)	ADVIA Centaur BNP (pg/mL)
4	2

f) Expected Results:

The expected values were determined from clinical studies performed for the predicate ADVIA Centaur BNP Test and results of the studies are included in the labeling for the ADVIA IMS BNP assay.

BNP concentrations in the Reference Group are shown in the tables below. The decision threshold was determined by the 95% confidence limit of BNP in the Reference population. The most appropriate decision threshold apparent from these distributions is 100 pg/mL. This BNP value translates into a general specificity of the test of greater than 97 %.

Reference Group

To establish the expected results, the circulating BNP concentration was determined from 1521 individuals without heart failure (785 women and 736 men). This population included apparently healthy individuals and individuals with hypertension, diabetes, renal insufficiency, and chronic obstructive pulmonary disease. The

descriptive statistics for BNP concentrations in the population without heart failure are shown in the following tables. These values are representative of the results obtained from clinical studies.

All	Age Group					
	All	<45 years	45-54 years	55-64 years	65-74 years	75 + years
Mean, pg/mL	23.2	11.9	15.6	19.5	28.3	60.3
SD, pg/mL	32.5	12.9	15.9	22.6	25.4	73.0
Median, pg/mL	14.5	8.6	10.4	13.8	22.1	43.7
95th Percentile, pg/mL	70.8	33.3	46.7	53.2	72.3	176
% < 100 pg/mL	97.4	99.7	99.7	98.8	97.0	85.5
Minimum, pg/mL	<2	<2	<2	<2	<2	<2
Maximum, pg/mL	576	128	119	286	164	576
N	1521	317	291	403	365	145

Males	Age Group					
	All	<45 years	45-54 years	55-64 years	65-74 years	75 + years
Mean, pg/mL	17.9	9.1	11.2	14.5	25.8	41.9
SD, pg/mL	22.9	9.4	11.8	13.9	25.1	48.8
Median, pg/mL	11.3	5.9	7.6	11.9	17.8	26.1
95th Percentile, pg/mL	54.3	29.4	32.8	38.8	67.6	121
% < 100 pg/mL	98.6	100	100	99.5	96.8	94.6
Minimum, pg/mL	<2	<2	<2	<2	<2	<2
Maximum, pg/mL	250	56.6	88.9	132	151	250
N	736	129	140	223	188	56

Females	Age Group					
	All	<45 years	45-54 years	55-64 years	65-74 years	75 + years
Mean, pg/mL	28.1	13.8	19.8	25.6	31.0	71.9
SD, pg/mL	38.8	14.6	18.0	29.0	25.5	82.9
Median, pg/mL	18.5	10.4	14.8	19.4	25.7	54.3
95th Percentile, pg/mL	86.1	35.9	56.7	75.5	72.9	167
% < 100 pg/mL	96.3	99.5	99.3	97.8	97.1	79.8
Minimum, pg/mL	<2	<2	<2	<2	<2	<2
Maximum, pg/mL	576	128	119	286	164	576
N	785	188	151	180	177	89

Patients with Heart Failure

To establish the expected results for the ADVIA Centaur BNP assay in individuals with heart failure, plasma samples were obtained from 722 patients diagnosed with heart failure (264 women and 458 men). The descriptive statistics

for BNP concentrations in patients with heart failure are presented in the following tables. These values are representative of the results obtained from clinical studies. Each laboratory should establish a reference range representing the patient population being evaluated. In addition, laboratories should be aware of their respective institution's current practice for the evaluation of heart failure.

Heart Failure Population – All

	NYHA Functional Class				
	All	NYHA I	NYHA II	NYHA III	NYHA IV
Mean, pg/mL	505	178	270	525	1134
SD, pg/mL	711	347	402	576	1141
Median, pg/mL	262	64.3	130	355	843
5th percentile, pg/mL	10.8	1.6	5.4	21.1	109
95th percentile, pg/mL	1873	772	999	1696	3157
% > 100 pg/mL	72.6	43.1	58.7	82.0	95.8
Minimum, pg/mL	<2	<2	<2	<2	4.0
Maximum, pg/mL	6989	2310	3107	4052	6989
N	722	72	242	289	119

Heart Failure Population – Males

	NYHA Functional Class				
	All	NYHA I	NYHA II	NYHA III	NYHA IV
Mean, pg/mL	518	121	308	542	1214
SD, pg/mL	726	135	475	588	1200
Median, pg/mL	245	77.7	135	339	950
5th percentile, pg/mL	10.7	3.9	4.4	23.2	71.5
95th percentile, pg/mL	1946	400	1280	1852	3157
% > 100 pg/mL	72.9	44.7	61.3	81.4	93.9
Minimum, pg/mL	<2	<2	<2	<2	33.7
Maximum, pg/mL	6989	552	3107	3503	6989
N	458	47	150	194	66

Heart Failure Population – Females

	NYHA Functional Class				
	All	NYHA I	NYHA II	NYHA III	NYHA IV
Mean, pg/mL	482	285	207	492	1034
SD, pg/mL	687	551	228	556	1068
Median, pg/mL	291	62.5	117	355	779
5th percentile, pg/mL	11.0	0	9.5	15.9	115
95th percentile, pg/mL	1575	1447	552	1518	2970
% > 100 pg/mL	72.0	40.0	54.3	83.2	98.1
Minimum, pg/mL	<2	<2	<2	4.8	4.0
Maximum, pg/mL	5845	2310	1231	4052	5845
N	264	25	92	94	53

These results show that there is a relationship between the severity of the clinical signs and symptoms of heart failure and the median BNP concentrations, demonstrating that the assay can be used as an aid in the diagnosis of all degrees of heart failure severity, including asymptomatic patients.

Andres Holle
Manager Regulatory Affairs
Bayer Corporation
511 Benedict Avenue
Tarrytown, New York 10591-5097

Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 13 2005

Mr. Andres Holle
Manger, Regulatory Affairs
Bayer HealthCare LLC
511 Benedict Avenue
Tarrytown, NY 10591

Re: k051265
Trade/Device Name: B-type Natriuretic Peptide (BNP) Assay for the ADVIA IMS
Regulation Number: 21 CFR 862.1117
Regulation Name: B-type natriuretic peptide test system
Regulatory Class: Class II
Product Code: NBC
Dated: May 12, 2005
Received: May 17, 2005

Dear Mr. Holle:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Carol C. Benson

Carol C. Benson, M.A.
Acting Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K051265

Device Name: B-type Natriuretic Peptide (BNP) Assay for the ADVIA IMS

Indications for Use:

The *Bayer ADVIA IMS* BNP method is for *in vitro* diagnostic use in the quantitative determination of B-type Natriuretic Peptide (BNP) in human plasma using the ADVIA IMS® System. This assay is indicated for the measurement of plasma BNP as an aid in the diagnosis and assessment of the severity of heart failure. In patients with acute coronary syndromes (ACS), this test, in conjunction with other known risk factors, can also be used to predict survival as well as to predict the likelihood of future heart failure. This assay is not intended for use on any other system.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K051265